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(71) **Applicant:**

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**Request for anonymity**

(56) **Documents taken into account in the evaluation of  
patentability:**

EP4 59 432 A1  
EP3 73 986 A1  
EP3 59 951 A1

**CHEMICAL ABSTRACTS, Vol. 112, No. 17:**

151358c:

EVANS T. W.:

i. a. Bleomycin-induced Lung Injury in the Rat:  
Effects of the Platelet-activating Factor (PAF)

Receptor Antagonist BN 52021 and Platelet  
Depletion. In: Environmental Health Perspectives,  
Vol. 88, 1990, pp. 65 – 69;

ITOKAWA, H.:

Et al.: Antitumor Principles from Ginkgo biloba L.  
In: Chem. Pharm. Bull., Vol. 35, 1987, pp.  
3016-3020;

(54)

**Use of a Drug for the Treatment of Metastatic Cancerous Diseases**

(57)

The invention relates to the use of ginkgolides which can be obtained from the leaves of the ginkgo biloba tree for the treatment of metastatic cancerous diseases. The therapeutic use lies in an amplification of the tumor growth-inhibiting effect of cytostatic chemotherapeutic agents as well as in a reduction of undesired effects after previous administration of the ginkgolides.

**The following specifications are taken from the documents filed by the applicant.**

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## Description

The invention relates to the use of ginkgolides for a therapeutic application in cases of metastatic cancerous diseases.

Preparations on the basis of a dry extract from leaves of the ginkgo biloba tree have been used for years for the treatment of various forms of disturbances of blood flow. Along with oral forms of administration, parenteral forms of administration also come into use.

The Ginkgo biloba extracts used therapeutically such as, e.g., the drug "Tebonin forte" from the Dr. Willmar Schwabe Company, contain ca. 24% flavonoids, 6% terpenoids (ginkgolides A, B, C, bilobalide), organic acids, and other groups of substances.

For the ginkgolides a large number of pharmacological effects have been described (P. Braquet et al.: Ginkgolides, J. R. Prous Science Publishers, Barcelona, ISBN: 84-404-1648-2), wherein ginkgolide B has proven itself as a particularly potent antagonist of the body's own platelet-activating factor.

The use of this type of dry extract from Ginkgo biloba for the treatment of metastatic cancerous diseases has been described (Laid-open Specification: P 38 32 056.8) wherein a potentiating effect of the cancer growth-inhibiting effect of various cytostatic agents was emphasized. Attribution of these effects to individual constituent substances of the Ginkgo biloba extract has not been done previously.

Hideji Itokawa et al. Chem. Pharm. Bull., Vol. 35(7), 3016-3020 (1987), and Chem. Pharm. Bull., Vol. 37(6), 1619-1621 (1989) describe a direct inhibiting effect of long-chain phenols from Ginkgo biloba on sarcoma 180 ascites in mice.

The invention consists of the use of ginkgolides or ginkgolide B for the treatment of metastatic cancerous diseases. Therein it is of importance that the ginkgolides are administered before the dose of the chemotherapeutic agents. This can be done orally as well as parenterally, where parenteral administration is to be given preference due to still unexplained bioavailability. A particularly high amplification of the tumor growth-inhibiting effect of cytostatic chemotherapeutic agents can be achieved by multiple prior administrations of ginkgolides.

Most metastatic tumors are incurable. The rise of tumor cells resistant to cytostatic agents limits the effectiveness of the chemotherapy. In the case of existing resistance to cytostatic agents the prior administration of ginkgolide leads to a renewed response to the cytostatic agents.

Ginkgolide B leads to characteristic changes in form of the membrane of the human red blood cell. It has still not been made clear whether membrane effects of this type are also to be observed in the tumor cell and whether these are responsible for the effect of amplifying the chemotherapy.

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## Claims

1. Use of a drug for the treatment of metastatic cancerous diseases characterized by the fact that the drug contains ginkgolides as the active ingredient.
2. Use according to claim 1 characterized by the fact that the ginkgolides are obtained from leaves of the Ginkgo biloba tree.
3. Use according to claim 1 characterized by the fact that ginkgolides A, B, and C in accordance with their natural occurrence in the leaves of the Ginkgo biloba tree are contained.
4. Use according to claim 1 characterized by the fact that only ginkgolide B is contained.
5. Use according to claim 1 characterized by the fact that the administration is always done before the dose of the chemotherapeutic agents.
6. Use according to claim 1 characterized by the fact that the tumor growth-inhibiting effect of cytostatic chemotherapeutic agents is amplified.
7. Use according to claim 1 characterized by the fact that the undesired effects of cytostatic chemotherapeutic agents are reduced.
8. Use according to claim 1 characterized by the fact that the administration can be done as an intravenous dose.
9. Use according to claim 1 characterized by the fact that the administration can be done per os.